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CLASSIFICATION OF CLINICAL FORMS OF BRUCELLOSIS

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[Figure and tables referred to are appended.]

In this paper, we are presenting a classification of the forms of brucellosis which we have used for 15 years, modifying it during this time as the need arose. In 1938 - 1939, this classification had already assumed its final form, after having been verified on a great number of clinical cases and after considerable material was collected by two expeditions into the region of the occurrence of *Bruc. melitensis*. It was published by us in 1941 in Klinicheskaya Meditsina and has since then been used in evaluating case histories, including cases of infection with *Bruc. abortus bovis*.

The principles which guided us in devising this classification are based first of all on a realization that the clinical aspects are closely connected with the pathogenesis of the disease. In other words, we discarded the static viewpoint in favor of the dynamic. The second principle to which we adhered is recognition of the importance of compensation of the infection process. The third principle involves assumption of four successive stages of the disease, a subdivision which is based on the study of a very great number of clinical cases. The four stages can be described as follows:

1. Incubation period, or the primary latent stage, which may continue for an indefinite time. In this stage, the pathogenic process is fully compensated.
2. The acutely septic stage, during which brucellosis assumes the form of a general septic infection. This stage is characterized by decompensation of the pathogenic process but lacks local affliction of various organs and systems.

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3. The secondary chronic stage, which is characterized by the formation of a number of local afflictions (metastases) and a chronic as well as recurrent clinical course. As soon as local foci of infection develop, there is decompensation of the pathogenic process, which alternates with subcompensation and occasionally even complete, although unstable, compensation.

4. The secondary latent stage, which is accompanied by full restoration of compensation and stable aftereffects of local afflictions or, more frequently, absence of such aftereffects. There may be recurrence of the previous stage if compensation is disturbed, or gradual disappearance of the infection, if compensation is retained.

Furthermore (and this is the fourth principle of our classification), we assumed that the disease may either pass through stage 2 or skip stage 2 entirely. When stage 2 is skipped, the appearance of the first clinical symptoms following stage 1 leads to a sustained primary chronic course of the disease. The primary chronic stage may then have a duration of several months or else continue up to 1-2 years or longer.

As a result of considering all of the factors mentioned above, we obtain five clinical forms of brucellosis: primary latent, acutely septic, secondary chronic, primary chronic, and secondary latent. These forms are shown in Table 1.

Moreover, one must take into consideration that both the groups of primary and secondary chronic metastatic forms can be subdivided into subgroups of clinically well-expressed or clinically indistinct cases. In the first subgroup of clinical cases, which are characterized by decompensation of the infection, fever continuing for several days is followed by sharply expressed local afflictions. In the second subgroup, characterized by subcompensation of the pathogenic process, the disease takes a slow and sluggish course, without the appearance of pronounced local foci. Furthermore, well-expressed forms may change into indistinct forms and vice versa.

The acute septic form may pass into the secondary latent form either through the secondary chronic metastatic form or through the septic metastatic form. If the disease takes the first course, the fever of the acute septic form ceases, but subfebrile fluctuations of the temperature remain: decompensation changes into subcompensation. The patients feel very well. Nevertheless, after the expiration of 1-2 months, the temperature again rises to a high level, and in a few days, some local involvement (affliction) sets in: the disease has assumed the secondary chronic form. If the disease takes the second course, the fever of the acute septic form does not stop, decompensation continues, and a local involvement develops very rapidly. The clinical picture comprises traits of both the acute septic and the metastatic form, one form merging into the other. The appearance of even a single metastasis indicates that the patient has already reached the third stage, the most severe stage of the disease.

On the basis of the preceding discussion, the following three forms of brucellosis may be added to the five forms enumerated above: primary chronic metastatic, secondary chronic metastatic, and septic metastatic. In other words, there are eight clinical forms of brucellosis.

On the basis of the system of classification given above, a typical diagnosis of an actual case of brucellosis will run as follows: brucellosis in the secondary chronic metastatic form accompanied by brucellar sacrolumbar radiculitis (or sacroiliitis, spondylitis, arthritis, orchitis, etc.). It is also necessary to indicate the degree of compensation.

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If the forms of brucellosis differentiated by us are actually distinct as far as the progress of the disease is concerned, they must exhibit typical immunobiological characteristics in addition to the clinical characteristics already mentioned. This was investigated by I. V. Seppi (who is an associate of our chair) under use of the reactions of Wright (agglutination), Huddleston (agglutination), and Buerne (allergic), as well as the so-called opsonophagocytary reaction. Huddleston's reaction is primarily of diagnostic significance: it is positive in 87-94% of brucellosis cases, irrespective of the form of the disease. It cannot characterize individual forms or indicate the intensity of the disease. The other three reactions proved more useful. The course of the opsonophagocytary reaction is particularly striking: it is very strong when the disease is in the primary latent form (average index equal to 48.8), showing complete compensation of the pathogenic process; drops sharply in the acute septic form (index, 26.6), showing decompensation; goes up again in the secondary chronic metastatic form (index, 30.4); and becomes still higher on restoration of compensation in the secondary latent form (index, 36). Clinically well-expressed primary and secondary forms do not differ from each other as far as the index of the phagocytary reaction is concerned (the index remains at the average level of 30.4), but the index goes up (to 33.6) in light and subcompensated forms.

The correlation between the three reactions mentioned above and the clinical forms of brucellosis is shown in Figure 1. One must conclude that forms of brucellosis which belong to distinct clinical types and represent various stages of the course of the disease also differ in regard to immunobiological indexes that are characteristic for them. Furthermore, hematological characteristics also permit differentiation between stages of brucellosis which correspond to different clinical forms (I. V. Seppi), and this differentiation is also possible on the basis of the reaction of complement fixation at 0° C (T. M. Torosov). Thus, the validity of our classification has been substantiated by both immunological and hematological data.

After establishing the validity of our classification, we may illustrate its practical applications as an aid in clarifying the nature and course of brucellosis infections. If we arrange brucellosis cases classified according to our scheme on the basis of percentual distribution both at the foci of infection and in hospitals, we obtain the over-all picture shown in Table 2. It is obvious that the most acute cases are concentrated in hospitals, while people who have the infection in a latent form are not hospitalized. From the data shown in Table 2, the differences in the course of infections caused by *Bruc. melitensis* and *Bruc. abortus bovis* are quite apparent. We may add that in cases of infections with *Bruc. melitensis*, we found that about 70% of the patients exhibited a state of decompensation, while about 30% were in a state of subcompensation. In infections with *Bruc. abortus bovis* on the other hand, only 8% of the patients exhibited decompensation and 15% subcompensation. The majority of patients (74%) did not even exhibit subcompensation, but rather what may be described as incomplete and unstable compensation. Thus, we may, with the aid of our classification scheme, characterize in a very specific manner the disease caused by *Bruc. abortus bovis* and use this knowledge of characteristic traits acquired in this manner to recognize infections produced by this particular causative factor. Hitherto, we knew only that *Bruc. abortus bovis* in general produces milder infections than *Bruc. melitensis*.

Furthermore, our classification scheme brings out a very important characteristic of the brucellosis infection, namely, that there is a considerable tendency toward compensation of the infection process. A great number of cases do not develop any clinical symptoms at all after the primary latent stage has been passed. A considerable number of patients do not reach the stage of complete disturbance of compensation and exhibit only subcompensation and indistinct forms of the disease. Even acutely septic forms of the disease result in spontaneous

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cures, i.e., the complete decompensation which is characteristic of such forms may change into complete compensation. The tendency toward compensation is more pronounced in *Bruc. abortus bovis* infections than infections with *Bruc. melitensis*. The latent stage of the disease may be very prolonged, as can be seen from the figures cited in Table 3, but cases continuing for 10-20 years are extremely rare. We have seen only five or six such cases and observed that they were interrupted by latent periods continuing for as long as 5-7 years. We are inclined to believe that what we observed were cases of complete recovery followed by re-infection.

It is noteworthy that the number of people found in any particular stage of the disease is inversely proportional to the duration of that stage (cf. Table 3). The tapering off of the number of cases with increasing duration indicates recovery: lethality from brucellosis is extremely low. While it is true that brucellosis is a chronic disease which affects human beings and guinea pigs for greater periods of time and in a more severe form than some other animals, this infection cannot be regarded as interminable and completely "acyclic". It runs through its stages and completes its course just as any other infection. Our system of classification is of value in contributing to our understanding of brucellosis as a disease which not only is not incurable, but even tends to disappear spontaneously in individuals affected by it.

[Appended figure and tables follow.]

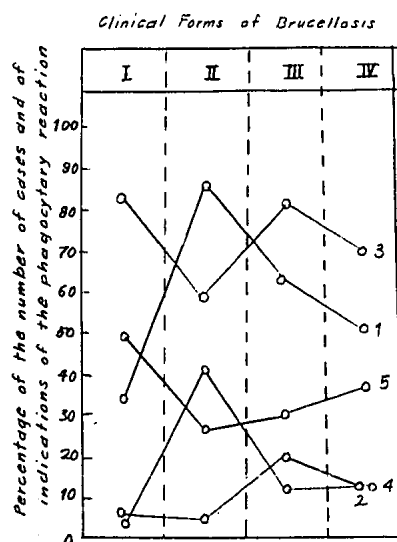


Figure 1. Dynamics of the Modification of Immunobiological Indexes in the Basic Clinical Forms of Brucellosis

Clinical Forms

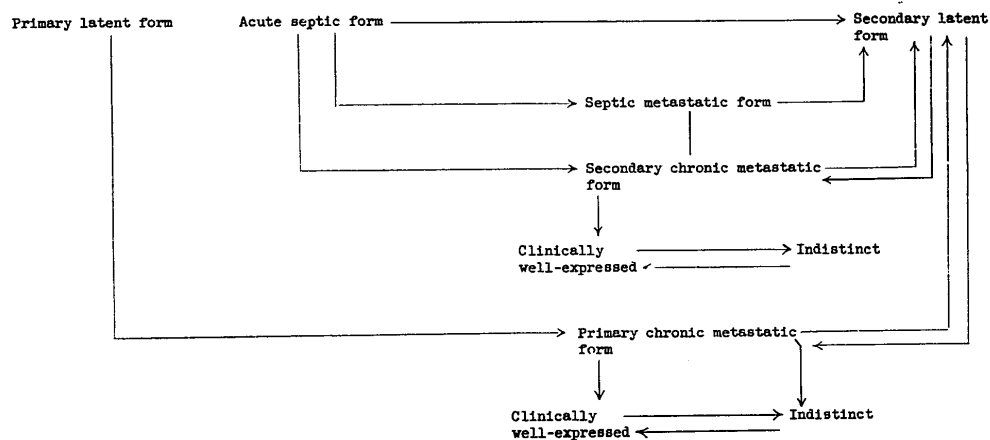
I. Primary latent. II. Acute septic. III. Secondary chronic metastatic.
IV. Secondary latent.

Reactions

Agglutination reaction: 1 - positive. 2 - sharply positive.
Allergic reaction: 3 - positive. 4 - sharply positive.
Phagocytary reaction: 5.

Table 1. Classification System of Clinical Forms of Brucellosis

- | | | | |
|------------------------------------|--|--|--|
| 1. Stage of compensated infection. | 2. Acute septic stage without local involvements (characterized by decompensation) | 3. Stage of subacute or chronic recurrent disease under formation of local involvements or afflictions (metastases) -- characterized by decompensation or sub-compensation | 4. Stage of restored or incomplete (unstable) compensation with or without after-effects |
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Table 2. Percentual Distribution of Clinical Forms of Brucellosis at Hospitals and Foci of Infection, Depending on Whether the Disease Is Caused by *Brucella melitensis* or *Brucella abortus bovis*

Causative Factor of Disease	<u>Form of the Disease</u>				
	<u>Primary Latent</u>	<u>Acute Septic</u>	<u>Secondary Chronic Metastatic</u>	<u>Primary Chronic Metastatic (well-expressed) (indistinct)</u>	<u>Secondary Latent</u>
Average Distribution at Hospitals					
	26	44	16	14	
Average Distribution at Foci of Infection					
<i>Brucella melitensis</i>	32	3	17	14	10
					23
Average Distribution at Hospitals					
	4	25	39	29	3
Average Distribution at Foci of Infection					
<i>Brucella abortus bovis</i>	69		17	10	4

Table 3. Total Duration of the Infection Process, the Clinically Well-Expressed Period of the Disease, and the Secondary Latent Stage (in percent of the total number of observed patients who were in the secondary latent stage)

Years:	Total Duration of the Infection Starting From the Appearance of the First Clinical Symptoms Until Diagnosis of the Disease in the Secondary Latent Stage			Duration of the Clinically Well-Expressed Period of the Disease			Duration of the Secondary Latent Stage		
	(Up to 3)	(3-6)	(6-8)	(Up to 3)	(3-6)	(6-8)	(Up to 3)	(3-6)	(6-8)
	56	38	6	90	10	0	74	24	2

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